REMARKS

Claims 1-5 are under prosecution in this case. Claims 4 and 5 have been amended for improved clarity. No new matter has been added in this Amendment.

Rejection under 35 U.S.C. 112:

Claims 1-3 remain rejected under 35 U.S.C. 112, first paragraph, on the ground that the Specification does not provide enablement for the scope of the claims. Applicants respectfully traverse this rejection.

The invention is a method of producing a biologically active factor VIII protein having modified glycosylation. The modified factor VIII protein produced by the invention is less likely to be antigenic and immunogenic when administered *in vivo*. The claims recite specifically that the factor VIII DNA be mutated to introduce the amino acid consensus sequence (N-X-S/T) for N-linked glycosylation and express the mutated DNA to obtain biologically active factor VIII. The as-filed Specification describes how this invention can be carried out stepwise using the leucine at residue 3 of SEQ ID NO:2 of the A2 domain as an example.

As pointed out by the Examiner, successful practice of the invention involves the ability to produce the factor VIII molecules that are biologically active. This limitation is clearly recited in claim 1. The biology of factor VIII was well established and numerous assays to measure the biological activity of factor VIII were readily available in the art at the time when the present application was filed.

It is alleged that the quantity of experimentation to practice the invention is large and undue. Applicant maintains that the kinds of the experimentation necessary to practice the invention are routine, not undue. The protocols for site-directed mutagenesis, protein expression using various cell culture systems, and testing of the newly produced modified factor VIII for its biological activity are well known and readily available in the art.

The Office Action cites Aly *et al.* to assert the unpredictability of the invention. However, the Aly *et al.* reference also points out that the role of carbohydrate in factor VIII function appears to be dispensable. For example, neuraminidase, beta-galactosidase, and N-glycanase did not inactivate factor VIII (see page 4936, left column, next to last paragraph, in the Discussion). This demonstrates that there is no reason to believe that a factor VIII molecule having modified glycosylation would be biologically inactive. The claimed invention is a method for producing a factor VIII having modified glycosylation that are biologically active.

Claims 4 and 5 are rejected under 35 U.S.C. as allegedly indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is based on the manner that the amino acid residue is recited in claims 4 and 5. Claims 4 and 5 have been amended to recite the correct residues in the present Amendment. Accordingly, this rejection is no longer relevant and withdrawal of the rejection is respectfully requested.

In summary, it is maintained that a person of ordinary skill in the art can make and use the claimed invention based on the description provided in the Specification, combined with the knowledge available in the art. Withdrawal of the rejection under 35 U.S.C. 112 is respectfully requested.

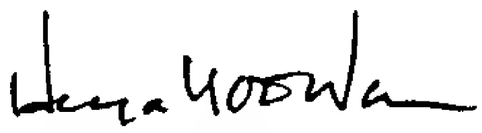
Conclusion:

Based on the foregoing amendments and remarks, it is believed that this case is in condition for allowance and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This Amendment is accompanied by a Request for Continued Examination, a Petition for Extension of Time (two months) and a check in the amount of $1140 in payment of the fees therefor. If the amount submitted is incorrect, please charge any deficiency or credit any overpayment to Deposit Account No. 07-1969.

Respectfully submitted,



Heeja Yoo-Warren
Reg. No. 45,495

GREENLEE, WINNER and SULLIVAN, P.C.
5370 Manhattan Circle, Suite 201
Boulder, CO 80303
Phone (303) 499-8080
Fax (303) 499-8089
ks: 12 December 2002 12/12/02
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Marked changes
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4. (Once amended) The method of claim 2 wherein said desired segment comprises the amino acid residue, leucine, at position [486] 3 of SEQ ID NO:2.

5. (Once amended) The method of claim 3 wherein said desired segment comprises the amino acid [residue] residues 2181-2222 [, glutamine, at position 2189] in the C2 domain of human factor VIII.